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TITLE: Interactive molecular conjugates

Abstract Paragraph Left (1):

The combination of the capabilities of stimuli-responsive components such as polymers and interactive molecules to form site-specific conjugates which are useful in a variety of assays, separations, processing, and other uses is disclosed. The polymer chain conformation and volume can be manipulated through alteration in pH, temperature, light, or other stimuli. The interactive molecules can be biomolecules like proteins or peptides, such as antibodies, receptors, or enzymes, polysaccharides or glycoproteins which specifically bind to ligands, or nucleic acids such as antisense, ribozymes, and aptamers, or ligands for organic or inorganic molecules in the environment or manufacturing processes. The stimuli-responsive polymers are coupled to the recognition biomolecules at a specific site so that the polymer can be manipulated by stimulation to alter ligand-biomolecule binding at an adjacent binding site, for example, the biotin binding site of streptavidin, the antigen-binding site of an antibody or the active, substrate-binding site of an enzyme. Binding may be completely blocked (i.e., the conjugate acts as an on-off switch) or partially blocked (i.e., the conjugate acts as a rheostat to partially block binding or to block binding only of larger ligands). Once a ligand is bound, it may also be ejected from the binding site by stimulating one (or more) conjugated polymers to cause ejection of the ligand and whatever is attached to it. Alternatively, selective partitioning, phase separation or precipitation of the polymer-conjugated biomolecule can be achieved through exposure of the stimulus-responsive component to an appropriate environmental stimulus.

Brief Summary Paragraph Right (10):

The combination of the capabilities of stimulus-responsive components and interactive molecules to form site-specific conjugates which are useful in a variety of assays, separations, processing, and other uses is disclosed. The polymers can be manipulated through alteration in pH, temperature, light, or other stimuli. The interactive molecules can be a biomolecule, such as (a) peptides or proteins, for example, antibodies, receptors, or enzymes, (b) polysaccharides or glycoproteins, or (c) nucleic acids such as antisense, ribozymes, and aptamers, all of which specifically bind to ligands or receptors, or a ligand for an organic or inorganic compound, for example, a metal chelating agent. The stimuli-responsive compounds are coupled to the interactive molecules at a specific site so that the stimulus-responsive component can be manipulated to alter ligand binding at an adjacent ligand binding site, for example, the antigen-binding site of an antibody or the active site of an enzyme. Binding may be completely blocked (i.e., the conjugate acts as an on-off switch) or partially blocked (i.e., the conjugate acts as a rheostat to partially block binding). Partial blocking can be used to effect selective binding, by still allowing small ligands to bind but totally blocking larger ligands.

Detailed Description Paragraph Right (39):

The stimuli-responsive components can be conjugated to a variety of different interactive molecules, including peptides, proteins, poly- or oligo-saccharides, glycoproteins, lipids and lipoproteins, and nucleic acids, as well as synthetic organic or inorganic molecules having a defined bioactivity, such as an antibiotic or antiinflammatory agent, and which bind to a target site, for example on a molecule such as a cell membrane receptor. In one preferred embodiment the interactive molecule is a protein genetically engineered to insert a coupling site for the stimulus-responsive component at a desired site. Examples of protein interactive molecules are ligand-binding proteins, including antibodies, lectins, hormones, and receptors, and enzymes. Other molecules which bind specifically or non-specifically to a target molecule include poly- or oligosaccharides on glycoproteins which bind to receptors, for

example, the carbohydrate on the ligand for the inflammatory mediators P-selectin and E-selectin, and nucleic acid sequences which bind to complementary sequences, such as ribozymes, antisense, external guide sequences for RNAase P, and aptamers.